

## Novel C–C Bond Cleavage of $\alpha$ -Azido Steroidal Ketones

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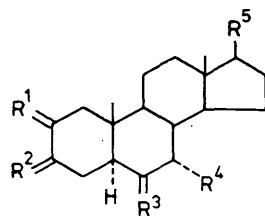
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**Summary**  $\alpha$ -Azido steroidal ketones were converted into  $\omega$ -cyano carboxylic acid derivatives with bromine in acetic acid at room temperature.

OUR interest in new synthetic approaches to biologically active steroidal alkaloids led us to investigate C–C bond cleavage of various  $\alpha$ -azido steroidal ketones. Thus far C–C bond cleavage reactions giving  $\omega$ -cyano carbonyl derivatives have been studied in the Beckman fragmentation of  $\alpha$ -substituted oximes<sup>1</sup> and in the nitrosolysis of ketones.<sup>2</sup> However, C–C bond cleavage of  $\alpha$ -azido ketones is unknown.

We report new C–C bond cleavage reactions of the steroidal  $\alpha$ -azido ketones (1)–(4) with bromine to provide

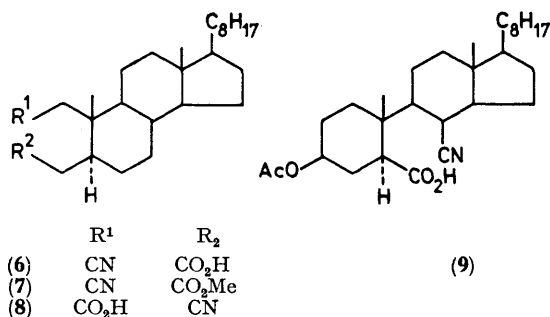


	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	R <sup>5</sup>
(1) <sup>3</sup>	$\alpha$ -N <sub>3</sub> , $\beta$ -H	O	H <sub>2</sub>	H	C <sub>8</sub> H <sub>17</sub>
(2) <sup>4</sup>	O	$\alpha$ -H, $\beta$ -N <sub>3</sub>	H <sub>2</sub>	H	C <sub>8</sub> H <sub>17</sub>
(3) <sup>3</sup>	H <sub>2</sub>	$\alpha$ -H, $\beta$ -OAc	O	N <sub>3</sub>	C <sub>8</sub> H <sub>17</sub>
(4) <sup>†</sup>	H <sub>2</sub>	$\alpha$ -H, $\beta$ -OAc	H <sub>2</sub>	H	COCH <sub>2</sub> N <sub>3</sub>
(5) <sup>‡</sup>	H <sub>2</sub>	$\alpha$ -H, $\beta$ -OAc	H <sub>2</sub>	H	CO <sub>2</sub> H

<sup>†</sup> The azido ketone (4) was synthesized from 3 $\beta$ -acetoxy-21-bromo-5 $\alpha$ -pregnan-20-one by Zbiral's method (ref. 3).

<sup>‡</sup> The carboxylic acid (5) was identified by comparison with an authentic sample.

$\omega$ -cyano-carboxylic acid derivatives. In a typical experiment, to a solution of 2 $\alpha$ -azido-5 $\alpha$ -cholestan-3-one<sup>3</sup> (1) (400 mg) in acetic acid (20 ml) was added bromine (150 mg) in acetic acid (10 ml) with stirring for 40 min at room temperature. Crystallization of the resulting oil from hexane-ether (9:1) gave (6) (310 mg), m.p. 171–174 °C, in



80% yield, which was identified on the basis of the following evidence. Its i.r. spectrum showed the presence of a carboxylic acid and nitrile group (2240 cm<sup>-1</sup>), its n.m.r. spectrum showed peaks at  $\delta$  2.50 (m, 4H, 1- and 2-CH<sub>2</sub>) and 8.84br (1H, CO<sub>2</sub>H), and its mass spectrum had peaks at  $m/e$  415 ( $M^+$ ), 375 (base peak,  $M^+ - \text{CH}_2\text{CN}$ ), 356 ( $M^+ - \text{CH}_2\text{CO}_2\text{H}$ ), 315 ( $M^+ - \text{C}_8\text{H}_7\text{CO}_2\text{H}$ ), and 302 ( $M^+ - \text{C}_8\text{H}_{17}$ ) (see fragmentation pattern in the Figure).

The seco-cyano carboxylic acid (6) was converted, in high yield, with HCl-MeOH into the corresponding methyl ester,

<sup>1</sup> R. K. Hill, *J. Org. Chem.*, 1962, **27**, 29; C. W. Shoppee and S. K. Roy, *J. Chem. Soc.*, 1963, 3774; A. Hassner and W. A. Wentworth, *Chem. Comm.*, 1965, 44; J. K. Paisley and L. Weiler, *Tetrahedron Letters*, 1972, 261; G. Rosini, A. Medici, and S. Cacchi, *Synthesis*, 1975, 665; D. Miljković and J. Petrović, *J. Org. Chem.*, 1977, **42**, 2101.

<sup>2</sup> M. M. Rogić, J. Vitrone, and M. D. Swerdloff, *J. Amer. Chem. Soc.*, 1975, **97**, 3848; M. M. Rogić, J. Vitrone, and M. D. Swerdloff, *ibid.*, 1977, **99**, 1156.

<sup>3</sup> A. Wolloch and E. Zbiral, *Tetrahedron*, 1976, **32**, 1289.

<sup>4</sup> E. Zbiral and G. Nestler, *Tetrahedron*, 1971, **27**, 2293.

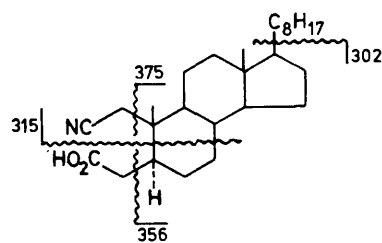


FIGURE.

(7), m.p. 88–89 °C, whose structure was also proved by spectral data. Results for other azido ketones are in the Table.

TABLE

Compd.	Recryst. solvent	M.p./°C	Yield, %
(5)	Ether	248–250	70
(6)	Hexane-ether	171–174	80
(8)	Hexane	162–164	71
(9)	Hexane	221–223	29

All products gave satisfactory analytical data. This method affords a new simple procedure for C–C bond cleavage of a variety of azido ketones, providing products with useful functional groups; it differs from conventional methods in that direct cleavage into cyano-carboxylic acid derivatives is accomplished.

We thank Professors Jisaku Kuroda, Machiko Tozawa, and Tsunetaka Kushimoto of the Jikei University School of Medicine for their interest and encouragement.

(Received, 24th February 1978; Com. 199.)